NDA 13-625/S-181
NDA 16-659/S-125
NDA 17-565/S-070
NDA 17-566/S-084
NDA 17-743/S-074
NDA 1 8-977/S-027

JAN 24 2000

Watson Laboratories, Inc.
Attention: Ernest Lengle, Ph.D.
Senior Director, Regulatory Affairs
311 Bonnie Circle
Corona, CA 92880

Dear Dr. Lengle:

Please refer to your supplemental new drug applications dated October 8, 1999, received October 12, 1999, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for:

NDA 13-625/S-18 1 Norinyl® 1 + 50 21 Day (norethindrone and mestranol) Tablets
NDA 16-659/S-125 Norinyl® 1 +50 28 Day (norethindrone and mestranol) Tablets
NDA 17-565/S-070 Norinyl® 1+35 21 and 28 Day (norethindrone and ethinyl estradiol) Tablets
NDA 17-566/S-084 Brevicon® 21 Day (norethindrone and ethinyl estradiol) Tablets
NDA 17-743/S-074 Brevicon® 28 Day (norethindrone and ethinyl estradiol) Tablets
NDA 18-977/S-027 Tri-norinyl® 21 and 28 Day (norethindrone and ethinyl estradiol) Tablets

Your submissions of October 8, 1999 constituted a complete response to our April 27, 1999 approvable action letter.

These supplemental new drug applications provide for:

1. Insertion of the following statement in the Physician Insert, **WARNINGS** section, T**hromboembolic Disorders and Other Vascular Problems** subsection, *d. Dose related risks of vascular disease from oral contraceptives subheading*

   "Products containing 50 mcg estrogen should be used only when medically indicated"

2. WATSONPHARMA has replaced the name Searle on the signature lines in the Physician Insert, Detailed Patient Labeling, and Brief Patient Summary due to the purchase of the referenced applications by Watson Laboratories, Inc. from Searle. The manufactured by statements and address have also been revised accordingly, to reflect the ownership change of the manufacturing site.

We have completed the review of these supplemental applications, as amended, and have concluded that adequate information has been presented to demonstrate that the drug products are safe and effective for use as recommended in the agreed upon labeling text and with the minor editorial revisions listed below. Accordingly, these supplemental applications are approved effective on the date of this letter.

Please reinsert the following text that was present and approved in your February 8, 1999 submission:

Detailed Patient Labeling

NON-CONTRACEPTIVE HEALTH BENEFITS section:

"Keep this and all medication out of the reach of children"

The final printed labeling (FPL) must be identical, and include the minor editorial revisions indicated, to the submitted draft labeling (Physician Insert, Detailed Patient Labeling, and Brief Patient Summary submitted October 8, 1999). These revisions are terms of the NDA approval.

Please submit 20 copies of the FPL as soon as it is available, in no case more than 30 days after it is printed to each application. Please individually mount ten of the copies on heavy-weight paper or similar material. For administrative purposes, these submissions should be designated "FPL for approved supplements NDA 13-625/S-181, 16-659/S-125, 17-565/S-070, 17-566/S-084, 17-743/S-074, and 18-977/S-027", respectively. Approval of these submissions by FDA is not required before the labeling is used.

If a letter communicating important information about this drug product (i.e., a "Dear Health Care Practitioner" letter) is issued to physicians and others responsible for patient care, we request that you submit a copy of the letter to this NDA and a copy to the following address:

MEDWATCH, HF-2
FDA
5600 Fishers Lane
Rockville, MD 20857

We remind you that you must comply with the requirements for an approved NDA set forth under 21 CFR 314.80 and 314.81.

If you have any questions, contact Jennifer Mercier, Regulatory Project Manager, at (301) 827-4260.

Sincerely,

Susan Allen, M.D., M.P.H.
Acting Director
Division of Reproductive and Urologic Drug Products
Office of Drug Evaluation III
Center for Drug Evaluation and Research